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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/044,708	10/22/2001	Yongchang Qiu	GH5412-1AUSA	7985

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EXAMINER	
WALLENHORST, MAUREEN	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 09/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/044,708	QIU ET AL.
	Examiner	Art Unit
	Maureen M. Wallenhorst	1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *14-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/22/01, 4/22/02*. + 1/7/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicants are notified that this application has been transferred to Examiner Maureen Wallenhorst in Art Unit 1743. The restriction requirement imposed by the previous Examiner has been changed to the following:

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-13, drawn to a method for enhancing protein identification and quantitation, classified in class 436, subclass 86.

II. Claims 14-20, drawn to a compound, classified in class 252, subclass 408.1.

3. The inventions are distinct, each from the other because:

Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in a materially different process of using that product which does not require mass spectrometry, such as a process of binding proteins to a solid support.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Perry Van Over on August 4, 2004, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-13. Affirmation of this election must be made by applicant in replying to this Office action. Claims 14-20 are

withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

6. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On line 4 of claim 1, the phrase "the disulfide bonds" lacks antecedent basis. Part b) of claim 1 is indefinite since it is not clear whether the linker is differentially labeled or the reagent as a whole is differentially labeled.

On lines 1-2 of claim 3, the phrase "wherein the reagent comprises a thiol-specific reactive group is selected from" does not make proper sense. This phrase should be changed to read: --wherein the thiol-specific reactive group is selected from--. On line 3 of claim 3, the word "or" should be changed to –and—so as to use proper Markush language.

On the last line of claim 5, it is suggested to change the phrase "wherein the reagent in the labeling step" to –wherein the reagent in the labeling step of the first sample—so as to provide further clarification.

In claim 8, the phrase "the hydrogen atoms" lacks antecedent basis.

On line 1 of claim 12, the full meaning for the abbreviation "MALDI-MS" should be recited since this is an independent claim. On line 3 of claim 12, the phrase "the disulfide bonds" lacks antecedent basis. Part c) of claim 12 is indefinite since it is not clear whether the reagent used to label the second sample is the same reagent defined in part b) used to label the first sample.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al (WO 00/11208, submitted in the Information Disclosure Statement (IDS) filed on October 22, 2001) in view of Brancia et al (submitted in the IDS filed on January 7, 2004).

Aebersold et al teach of a method for the quantitative analysis of proteins in mixtures. The method involves the use of affinity-labeled protein reactive reagents that allow for the selective isolation of peptide fragments. The isolated peptide fragments are characterized by mass spectrometric techniques such as matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS). See the top of page 17 in Aebersold et al. The method comprises the steps of reducing the disulfide bonds of proteins in a sample to produce free thiol (SH) groups, digesting the proteins with trypsin to form peptides, and reacting the peptides with an affinity-labeled protein reactive reagent. The affinity label is preferably biotin, which is attached to a thiol-specific reactive group via a linker. The thiol-specific reactive group can be a haloacetyl group or a maleimide. The linker may comprise acidic or basic groups such as COOH groups. The reagent can be isotopically labeled by substitution of the linker atoms with stable isotopes (i.e. deuterium). See the structures of the compounds on the bottom of pages 75 and 76 of Aebersold et al where the structure on page 75 shows an affinity-labeled protein reactive reagent containing a haloacetyl thiol-reactive group attached to a linker and the structure on page 76 shows an affinity-labeled protein reactive reagent containing a maleimide thiol-reactive group attached to a linker. In the method, one sample of peptides is combined with a labeled form of the reagent (i.e. isotopically heavy form), and a second sample is combined with an unlabeled form of the reagent (i.e. isotopically light form). Aliquots of the samples labeled with the isotopically different reagents (i.e. heavy and light reagents) are then combined. Excess affinity

tagged reagent is then washed away, and the tagged peptides are run through a separation column containing a capture reagent for the tagged peptides in order to separate the peptides from the sample. The separated peptides are then analyzed using a mass spectrometry method such as MALDI-MS. Aebersold et al fail to teach that the affinity label on the reagent can be a guanidino group.

Brancia et al teach of a method for improved matrix-assisted laser desorption/ionization mass spectrometry. In the method, proteins are digested with trypsin to form peptides. The lysine residues on the peptides then undergo guanidination to convert the lysine residues to homoarginine residues since peptides containing arginine having a guanidine functionality produce more intense MALDI signals and an improved response factor than peptides containing lysine, thereby allowing for better identification and quantitation of the peptides. Brancia et al teach that the conversion of peptides to contain an arginine group with a guanidine functionality allows for the improved detection of peptides otherwise yielding signals of minor abundance in MALDI-MS, and enhances the capability of protein mixture analysis by MALDI-MS. See pages 2070 and 2073 in Brancia et al.

Based upon the combination of Aebersold et al and Brancia et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute an arginine group having a guanidine functionality for the biotin affinity label in the affinity-labeled protein reactive reagent taught by Aebersold et al since Aebersold et al teach that the peptides are analyzed by MALDI-MS, and Brancia et al teach that an arginine group with a guanidine functionality allows for the improved detection of peptides otherwise yielding signals of minor

abundance in MALDI-MS, and enhances the capability of protein mixture analysis by MALDI-MS.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Goodlett et al and Figeys et al who teach of methods for labeling proteins for protein quantitation and identification.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Wednesday from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

September 27, 2004

Maureen M. Wallenhorst
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PRIMARY EXAMINER
GROUP [redacted] 1700